

Please replace the paragraph on page 17, lines 17-25 with the following new paragraph:

By using the Affymetrix chips (GENECHIP® Human Genome U133 Set), the inventors of the present invention identified the down-regulated nucleic acid marker sequences that have shown at least about two-fold decrease in expression levels in biological samples from disease cells and/or tissue, including colon cancer-derived cells and/or tissue, relative to the expression level in samples from normal cells and/or tissue, e.g., normal colon tissue and/or normal non-colon tissue. Table 1 describes the identified nucleic acid marker sequences that are down-regulated in tumor cells and/or tissue, e.g., colon cancer-derived cells and/or tissue. The sequences dictated by SEQ ID NO's are genomic sequences of the corresponding genes.

Please replace the paragraph on page 17, lines 28-30 with the following new paragraph:

Gene name	GENBANK® ID	UNIGENE™ ID	Cancer		Normal		
			Mean	Median	Mean	Median	SEQ ID

Please replace the paragraph on page 26, lines 14-35 with the following new paragraph:

Gene name	GENBANK® ID	UNIGENE™ ID	# CpG islands	Search parameter	SEQ ID NO
PYY	NM_004160.1	Hs.169249	2	1000-exon1+1000	130
ANPEP	NM_001150.1	Hs.1239	1	1000-exon1+1000	131
SLC26A2.a	AI025519	Hs.29981	3	1000-exon1+1000	132
MT1K	R06655	Hs.188518	1	1000-exon1+500	133
MMP28	NM_024302.1	Hs.231958	2	1000-exon1+500	134
FLJ21511	NM_025087.1	Hs.288462	1	1000-exon1+500	135
ATOH1	NM_005172.1	Hs.247685	3	1000-exon1+500	136
PDE9A	NM_002606.1	Hs.18953	3	1000-exon1+500	137
CA4	NM_000717.2	Hs.89485	1	1000-exon1+500	138
EDN3	NM_000114.1	Hs.1408	1	1000-exon1+500	139
SGK	NM_005627.1	Hs.296323	8	1000-exon 1-4 +500	140
HPGD	U63296.1	Hs.77348	1	1000-exon1+500	141

Please replace the paragraph on page 49, lines 2-14 with the following new paragraph:

Twenty well characterized, microdissected samples of colorectal cancer tissue were obtained from consenting patients. A second set of twenty, microdissected samples of normal adjacent colon tissue were also obtained. Total RNA was extracted from these samples using RNEASY® kits (QIAGEN, Valencia, CA) according to the manufacturer's instructions. Expression profiling was performed using the GENECHIP® expression arrays from Affymetrix (Santa Clara, CA). Reverse transcription, second-strand synthesis, and probe generation was accomplished by standard Affymetrix protocols. The Human Genome U133A GeneChip, which contains more than 15,000 substantiated human genes, was hybridized, washed, and scanned according to Affymetrix protocols. Changes in cellular mRNA levels in the cancerous tissues were compared with mRNA levels in the normal colon tissues. GENESPRING® v4.2 (Silicon Genetics, Redwood City, CA) was used to normalize and scale results and compare gene expression levels in the cancer tissue relative to that in the normal tissue.

Please replace the paragraph on page 51, lines 18-25 with the following new paragraph:

PCR amplification for sequencing: Primers were designed to amplify both methylated and unmethylated fragments of DNA (Table 5). Five  $\mu$ L of modified DNA (1/10 of modification reaction) was amplified first in a 25 $\mu$ L reaction volume containing 10mM Tris-HCl pH8.3, 50mM KCl, 1.5mM to 2mM MgCl<sub>2</sub>, (Applied Biosystems), 0.25mM each dNTP, 0.5 unit AmpliTaq® (Applied Biosystems), and sequencing primers (each at 200nM). Cycling conditions were 10 minutes at 95°C, 40 cycles of 30 seconds at 95°C, 30 seconds at 54-62°C, 30 seconds at 72°C, subsequently followed by extension for 5 minutes at 72°C.

Please replace the paragraph starting on page 51, line 26 and ending on page 52, line 3 with the following new paragraph:

Reaction products were purified either by the shrimp-alkaline phosphatase-Exo1 standard method or on the Qiagen Qiaquick™ PCR clean-up column and eluted in 30 $\mu$ L 10mM Tris-HCl, pH8.5. The amount of DNA was determined by absorbance at OD<sub>260</sub> and stored at -20°C before sequencing. Purified amplicons were sequenced by the chain-termination sequencing method. Reverse sequencing primers at 3.2 $\mu$ M concentration and 200ng of each purified amplicon diluted in 10 $\mu$ L dH<sub>2</sub>O were sent to a commercial sequencing service (SeqWright).

Please replace the paragraph on page 56, lines 17-24 with the following new paragraph:

Further support for the clinical importance of these sites comes from the changes seen in gene expression of the genes after treatment of cell lines with 5-aza-2'-deoxycytidine. These values were obtained from Affymetrix expression profiling of treated and untreated cell lines using the procedure described above. Genes that had at least one cell line that showed a restoration of gene expression of 2-fold or greater after treatment with the demethylating agent were selected. Examples of expression restoration was seen for SCNN1B (cell line LS123 at 4.1-fold), CA4 (cell line at LS174T 2.8), and GPX3 (cell line LS174T at 8.5-fold).